REMARKS

In order to clarify the prosecution history of the instant application and to expedite the prosecution of the newly added claims, Applicants offer the following remarks. In the Office Action mailed 6/5/01, the Examiner restricted the then pending claims into six groups and two species. **Group I** was directed to a composition containing an electrode, at least one nucleoside, and a conductive oligomer as well as methods for making the same. **Group II** was directed to electrode based methods of detecting a target nucleic acid sequence. **Group III** was directed to methods for attaching a conductive oligomer to a gold electrode. **Group IV** was directed to a conductive oligomer. **Group V** was directed to a composition containing a nucleoside and a conductive oligomer. **Group VI** was directed to a peptide nucleic acid attached to a monomeric unit. Group VI was further divided into two species: **Specie VIA**, directed to peptide nucleic acids without an attached electrode, and **Specie VIB**, directed to peptide nucleic acids with an attached electrode. According to the Examiner, the species were separated in this manner as "[t]he presence or absence of an electrode on the peptide nucleic acid are distinct species as the direct any usage to electrode assay methods versus solution assay methods or other uses which do not require an electrode for measurement.

In response to the restriction requirement the Applicants elected Group VI, and Specie VIB. However, during later prosecution, new claims were added that expanded the scope of the attached substituent to include electron transfer moieties (ETMs) rather than merely electrodes. The Examiner has allowed prosecution on the merits of these claims to continue, in contrast to claims directed fluorescent label substituents which were rejected as relating to a non-elected invention. See Office Action mailed 2/06/03, page 3. Accordingly, Applicants believe the currently pending claims, Claims 47-49, 51-53 and 60-61, are consistent with the election filed November 2, 2001, as further expanded by the Examiner.

Title

The title of the invention stands objected to as not descriptive of the invention as presently claimed. As the title has been amended, see above, withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

Claims 47-49 and 51-53 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Meade et al., WO/95/15971. In particular, the Examiner asserts that Meade teaches methods for the site specific addition of electrodes to nucleic acids, including nucleic acid analogs, in a variety of positions. *See e.g.,* page 20, lines 18-20; Fig. 4A; page 20, lines 30-34; page 21, line 1; page 24, line 16; page 22, lines 7-9; page 24, line 18; and page 22, lines 17-20. In addition to the attachment of transition metals to conventional sugar-phosphate backbones, the reference discloses that transition metals can be added to nitrogen or sulfur atoms as part of nucleotide dimers that are linked by peptide bonds. *See e.g.,* page 32, lines 30-32.

The present claims are directed to the modification of peptide nucleic acids in which an ETM is covalently attached to an α-carbon (*See e.g.,* Figs. 31A and 31B) or base of a monomeric subunit. As distinguished from the linkages disclosed in Meade, the specific linkages of the present invention are characterized by the attachment of an ETM to a specific α-carbon or base within a monomeric subunit of a peptide nucleic acid. The Examiner is reminded that a species (in this case, attachment to the α-carbon of a peptide nucleic acid monomer) can be patentable over a genus (e.g. an ETM attached to a nucleic acid analogue such as a peptide nucleic acid). *See, In re Duel*, 34 USPQ2d 1210, 1215 (Fed Cir. 1995) (general knowledge of cDNA molecules based on known protein sequence (genus) does not render specific cDNA molecules (species) obvious).

It is well settled law that in order to anticipate a claim, a single prior art reference must expressly or inherently describe each and every element set forth in the claim. *See Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051 (Fed. Cir. 1987). Moreover, "[t]he identical invention must be shown in as complete a detail as is contained in the claim" See M.P.E.P. 2131. As stated by the Federal Circuit, "for a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." *See In re Bond*, 15 USPQ2d 1566.

As discussed above, Meade does not explicitly disclose linkages between ETMs and α-carbons or bases within monomeric subunits of peptide nucleic acids. Accordingly, Applicants respectfully request withdrawal of the instant rejection.

Claims 47-49 and 51-53 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Megerle et al., U.S. Patent No. 5,874,046. Megerle discloses the same techniques taught in Meade. Column 1, lines 56-65 and Column 4, lines 47-61.

The present invention is summarized above.

The arguments set forth above for the Meade reference apply equally to Megerle. Like Meade, Megerle does not disclose linkages between ETMs and α-carbon or base positions within the monomeric subunits of peptide nucleic acids. Applicants accordingly respectfully request that the 35 U.S.C. § 102(e) rejection of claims 47-53 be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

Claims 47-49, 51, 53, 60 and 61 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Mirkin et al., U.S. Patent No. 6,361,944. In particular, the Examiner asserts that Mirkin teaches nanoparticles with attached oligonucleotides, that these oligonucleotides may be modified by the addition of ferrocene (column 34, lines 2-32), and suggests the substitution of peptide nucleic acids for the disclosed oligonucleotides (column 42, lines 4-14). As a preliminary matter, Applicants do not admit that Mirikin is a proper 103(a) reference, as Mirkin relies on at least two continuation-in-part applications for its priority date and support for the subject matter cited by the examiner may not be present in those prior applications. Assuming, arguendo, that Mirkin could be considered a proper prior art reference, Mirkin only describe the addition of ferrocene to the nanoparticles in three ways: (1) as part of a ferrocene-derivatized phosphoramadite which would "end-label" an attached oligonucleotide (citing, Mucic et al., *Chem. Commun.*, 55 (1996); Eckstein, ed., in *Oligonucleotides and Analogues*, 1st ed., Oxford University, New York, NY (1991)); (2) as a part of a polymer bound to the nanoparticle separately from the oligonucleotide (citing, Watson et al., *J. Am. Chem. Soc.*, 121, 462-463 (1999)); or (3) the ferrocene-modified polymer of (2) could be employed as a portion of a co-polymer which also included the oligonucleotide (citing, Moller et al., *Bioconjugate Chem.*, 6, 174-178 (1995)). None of these methods of ferrocene incorporation teach or suggest attachment at the α-carbon or a base position within a monomeric subunit of peptide nucleic acids.

The instant invention is described above.

To establish a *prima facie* case of obviousness the prior art reference (or references when combined) must teach or suggest all the claim limitations. In addition, the teaching or suggestion

to make the claimed combination must be found in the prior art, and not based on applicant's disclosure. *See*, *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) M.P.E.P. §2143.

As discussed above, Mirikin does not teach or suggest attachment of an ETM at the α-carbon or at a base position within a monomeric subunit of peptide nucleic acids. Accordingly, withdrawal of the instant rejection is respectfully requested.

CONCLUSION

Applicants submit that the application is in form for allowance and early notification of such is requested. If the Examiner believes that any unresolved issues may be disposed of by telephone, he is respectfully requested to call the undersigned at (415) 781-1989. This paper is filed under 37 C.F.R. section 1.34(a).

Dated: 12/10/03

Respectfully submitted,

DORSEY & WHITNEY, LLP

By: Renee M. Kosslak

Renee M. Kosslak, Reg. No 47,717 for
Robin M. Silva, Reg. No. 38,304

Filed under 37 C.F. R. § 1.34(a)

Four Embarcadero Center
Suite 3400
San Francisco, California 94111-4187
Telephone: (415) 781-1989
Fax No. (415) 398-3249

1124661